R15 is any amino acid other than Pro, other than a conserved amino acid replacement, or Cys;

R16 is Cys, or any other amino acid;

R17 is Trp or a conserved amino acid, an analog of Trp, an amino acid having an aromatic side group, any amino acid other than Trp, other than a conserved amino acid replacement, an amino acid lacking an aromatic side group, deleted, or Cys;

R18 is Gln or a conserved amino acid, Glu or a conserved amino acid, Trp or a conserved amino acid, an analog of Trp, an amino acid having an aromatic side group, any amino acid other than Trp, other than a conserved amino acid replacement, an amino acid lacking an aromatic side group, or deleted;

R19 is Val, a conserved amino acid, or deleted;

provided that: if $R^6$ is Cys, then $R^{15}$ is Cys, the disulfide bridge is formed between the two, and $R^7$, $R^8$, $R^{16}$ and $R^{17}$ are not Cys; if $R^7$ is Cys, then $R^{16}$ is Cys, the disulfide bridge is formed between the two, and $R^6$, $R^8$, $R^{15}$ and $R^{17}$ are not Cys; if $R^8$ is Cys, then $R^{17}$ is Cys, the disulfide bridge is formed between the two, $R^6$, $R^7$, $R^{15}$ and $R^{16}$ are not Cys, and $R^{18}$ is Trp or a conserved amino acid, an analog of Trp, an amino acid having an aromatic side group, any amino acid other than Trp, other than a conserved amino acid replacement, an amino acid lacking an aromatic side group, or deleted.

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~~29.~~ (New) A method of inhibiting appetite or weight gain in a subject, comprising:

identifying a subject in need of inhibiting appetite or weight gain; and

administering an effective amount of an antagonist of melanocyte concentrating hormone (MCH) to said subject, wherein the antagonist is a peptide analog of MCH, and wherein the peptide analog has one to ten amino acid residues of MCH which have been substituted or deleted,

thereby inhibiting appetite or gain of weight in a subject.

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## REMARKS

Claims 8-29 are pending. Claim 8 has been amended. New claims 13-29 have been added. The new claims and the amendments to claim 8 are supported throughout the application as filed, e.g., at page 15, lines 1-5, and page 24, line 16, to page 26, line 10. The amendments to the specification were made merely to address informalities. No new matter has been added.

Priority

The specification has been amended to contain a specific reference to the prior application to which this application claims the benefit of an earlier filing date.

Objection To The Disclosure

The abstract of the disclosure has been amended as suggested by the Examiner.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claim 8-12 are rejected under 35 U.S.C. § 112, first paragraph, as "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." The Examiner states,

> [t]he claims are not commensurate in scope with the specification. Applicant should note that the claims encompass such things as drinking water or eating low calorie food due to the definition of "MCH antagonist" in the specification.

Claim 8 has been amended to recite administering an MCH antagonist wherein the antagonist is a peptide analog of MCH. Terefore, the present claims do not encompass such things as drinking water or eating low calorie food.

Moreover, the Examiner alleges the following.

> The instant specification fails to identify a single compound which is derived from MCH which acts as an antagonist and inhibits eating, appetite or gain of weight. The instant application discloses that MCH promotes eating behavior. The specification indicates that MCH could be altered or modified in order to generate a compound which acts as an antagonist of MCH (see page 24 of the specification). However, one of ordinary skill in the art does not have a reasonable expectation that any one embodiment encompassed by the generic formula found in the specification would function in the manner required by the claims, absent evidence to the contrary. For example, at page 21 of the specification, it is stated that MCH(5-15) is sufficient to elicit a response equipotent to native MCH. Then at page 26, MCH (5-16) is indicated to be an antagonist of MCH. This is inconsistent in that the specification indicates that the amino acid at position 16 is not required for activity of MCH, but then the specification further states that if it is present, the molecule will be an antagonist.

> Based on this disclosure, one of ordinary skill in the art would not know which forms of the modified MCH would act as an antagonist without first making and testing each possible mutant. Although the specification teaches which amino acids would be critical for the biological activity of MCH, the disclosure as to which amino acids would be critical for antagonistic activity contradict these statements. Therefore, the specification does not provide clear guidance as to which amino acids (i.e. structural elements) of the native protein are critical to the biological activity of an antagonist and which amino acids should be altered in order to obtain an MCH antagonist.

Applicant strongly disputes the Examiner's assertion that the "specification fails to identify a single compound which is derived from MCH which acts as an antagonist." On the contrary, Applicant has identified, in detail, the structure of peptides useful as MCH antagonists and the identity of critical residues (see, e.g., pages 24-25). These teachings clearly distinguish the structure of an MCH peptide analog which acts as an agonist from one which acts an antagonist, and provides clear guidance as to which amino acids of the native protein should be altered in order to obtain an MCH antagonist. For example, the specification teaches that an agonist has a Val or a conserved substitution at position R12 (page 23, line 23), while an antagonist has an amino acid other than Val or a conserved substitution at the same position (page 25, line 3). Similar teachings are given with respect to various other residues, e.g., the residues at position R13, R14, and R15.

In addition, Applicant has listed numerous preferred peptide analog antagonists (see, e.g., page 26, lines 1-10). This list is consistent with other teachings in the application, since the list clearly refers to analogues of MCH that are within the structural parameters described in the immediately preceding paragraphs. Therefore, it would be clear to one skilled in the art that the fragments listed, e.g., MCH(1-16), refer to the corresponding length of the preferred antagonist analogues, and not to fragments of the native peptide, as the Examiner appears to misunderstand. Thus, contrary to the Examiner's assertion, the specification does not indicate that if an amino acid is present at position 16, the molecule will be an antagonist. Rather, the specification teaches that a preferred antagonist is a peptide analog having the structural parameters taught in pages 24-25, and corresponding to MCH residues 1-16. Further, the specification teaches various methods of preparing MCH peptide analogs (see, e.g., page 15, lines 1-30), numerous assay procedures which broadly enable the identification of MCH peptide antagonist activity

(see, e.g., pages 15-18), and methods for making large numbers of peptide variants, which are known in the art (see, e.g., pages 31-39). Based on these teachings, one of skill in the art would have ample guidance to make and use the claimed invention.

Moreover, Applicant has subsequently confirmed that antagonizing MCH leads to inhibition of appetite or inhibition of weight gain. Applicant has produced MCH "knock out" transgenic mice, and found that such mice show decreased appetite and low weight.

Therefore, for the reasons discussed above, Applicant respectfully requests that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 8-12 are rejected under 35 U.S.C. § 112 as "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

Claim 8 is said to be indefinite in the use of the term "MCH." Claim 8 has been amended to spell out "melanocyte concentrating hormone" before the use of the abbreviation "MCH."

Claim 8 is said to be indefinite in the recitation of "a method of inhibiting eating appetite." Claim 8 has been amended to delete the word "eating" as suggested by the Examiner.

Rejections Under 35 U.S.C. § 102

Claims 8-11 are rejected under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,126,332 (Ohta et al.). The Examiner states,

> Ohta et al. disclose a method of inhibiting eating and appetite in a subject by administering a composition comprising casein and water-soluble dietary fiber (see claims). The instant claims require the administration of an antagonist of MCH, wherein the instant specification defines an antagonist of MCH as "agents which result in an inhibition of feeding behavior". Therefore, the composition of Ohta et al. meets the limitations of the instant claims as being an MCH antagonist.

As amended, claim 8 recites that an antagonist of MCH is a peptide analogue of MCH. Ohta et al. do not describe the use of peptide analogues of MCH, thus Ohta et al. do not anticipate the presently claimed invention. Therefore, Applicant respectfully requests that this rejection be withdrawn.

In addition, claims 8-12 are rejected under 35 U.S.C. § 102(b) based on a public use or sale of the invention. The Examiner asserts that,

> The instant specification defines an antagonist of MCH as being anything that inhibits eating appetite or the gain of weight. Therefore, the claims are directed to a method of inhibiting eating appetite or the gain of weight by anything that inhibits eating appetite or the gain of weight. The public has been practicing the claimed method for hundreds of years in that the eating of low calorie food or reducing the intake of food will inhibit the gain of weight.

As amended, claim 8 recites that an antagonist of MCH is a peptide analogue of MCH, thus obviating this rejection.

Rejections Under 35 U.S.C. § 103

Claims 8 and 12 are rejected as being unpatentable over Ohta et al. under 35 U.S.C. § 103. The amendments to claim 8 obviate this rejection. Ohta et al. do not teach or suggest the presently claimed invention. Therefore, Applicants respectfully request that this rejection be withdrawn.

Applicants submit that all of the claims are now in condition for allowance, which action is requested. Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 1/22/01

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